

Claims 16-17, 45-46, 73-74, 93-94, 103, 113-114, 123, and 133-134 were previously canceled.

Claims 3-11, 19-24, 32-40, 48-53, 60-68, 76-81, 88-91, 96-101, 108-111, 116-121, 128-131, 136-141 and 148-150 have been withdrawn from consideration due to the election-of-species requirement set forth in the Office Action mailed on April 11, 2003.

Claims 1-2, 12-15, 18, 25-31, 41-44, 47, 54-59, 69-72, 75, 82-87, 92, 95, 102, 104-107, 112, 115, 122, 124-127, 132, 135, 142-147, and 151-163 are currently under examination.

Independent claims 1, 30, 58, 86, 106, and 126 have each been currently amended to include, as concentration-enhancing polymers, hydroxypropyl methyl cellulose phthalate and hydroxypropyl methyl cellulose acetate succinate. These two polymers were previously included in dependent claims 18, 47, 75, 95, 115, and 135 but were omitted from the independent claims by oversight. The aforementioned dependent claims support the amendment, as does the text at page 42, lines 28-29.

Each of independent claims 1, 30, 58, 86, 106, and 126 has also been currently amended to state that the drug has an aqueous solubility less than about 1 mg/mL. Support is in the specification at page 26, lines 13-22.

The Invention

The invention relates to compositions that increase the concentration of low solubility drugs, i.e., those having an aqueous solubility less than about 1 mg/mL. The solubility-improved form of the drug when dissolved in the use environment provides an initial concentration of drug that exceeds the equilibrium concentration of drug, while the concentration-enhancing polymer retards the rate at which the initially enhanced drug concentration falls to the equilibrium concentration. See page 12, lines 22-28 of the specification.

The §112 Rejection

Claims 146 and 155, and certain claims dependent therefrom, were rejected under 35 U.S.C. §112, second paragraph, as indefinite. The Examiner stated that

“Part (c) of claim 146 and part (d) of claim 155 are confusing. Claim 146 is examined as an aqueous solution that contains a drug and concentration-enhancing polymer, where at least a portion of the drug in solution is associated with at least a portion of the polymer to form drug-polymer particles having a size of from about 10

nanometers to about 1000 nanometers, and the concentration of drug in the solution is at least 1.25-fold the equilibrium concentration of said drug. [Pages 6-7 of the Office Action]

Much of the forgoing language in the rejection was reproduced from claim 146, part (b). Although the Examiner requested that Applicants' look at claims 146 and 155, with emphasis on parts (c) and (d) and the claims in general, it remains unclear to Applicants what the basis for the rejection is or why the claim language is indefinite and/or unclear. It is simply untenable that one skilled in the art (to whom §112 is addressed) would not understand Applicants' claim language, particularly in view of the extensive disclosure and explanation that Applicants supplied in the application. See, for example, the textual material starting at page 16, line 28 and extending over to page 21, line 30.

Part (c) of claim 146 is reproduced as follows:

- (c) said solution having a maximum concentration of said drug that is at least 1.25-fold an equilibrium concentration of said drug in said use environment, and a concentration of said drug that exceeds said equilibrium concentration for a longer time than the concentration of said drug in said use environment provided by a control composition exceeds said equilibrium concentration, wherein said control composition is free from said concentration-enhancing polymer and comprises an equivalent quantity of said drug in said solubility-improved form.

Part (d) of claim 155 is reproduced as follows:

- (d) said solution having a maximum concentration of said drug that is at least 1.25-fold an equilibrium concentration of said drug in said use environment, and a concentration of said drug that exceeds said equilibrium concentration for a longer time than the concentration of said drug in said use environment provided by a control composition exceeds said equilibrium concentration, wherein said control composition is free from said concentration-enhancing polymer and comprises an equivalent quantity of said drug in said solubility-improved form.

It is assumed that the Examiner is maintaining the rejection as it was stated and reasoned in previous office actions, i.e., that the term "solution" is unclear because it is not explained how the solution is formed in a use environment such as in vitro and in vivo. As a preliminary matter, it is emphasized that Applicants have abundantly explained the role played by solubilization and by precipitation-inhibition in their specification. Again, note the text in Applicants' specification at page 16, line 28, extending over to page 21, line 30.

Applicants otherwise continue to traverse the rejection on the same basis as previously argued, i.e., it matters only whether one skilled in the art would understand Applicants' claims when read in light of the specification. See Mossman v. Broderbund Software Inc., 51 USPQ2d 1752, 1757 (E.D. Michigan 1999)

...The 'definiteness' requirement means that a claim must have a clear and definite meaning when construed in light of the complete patent document....A claim complies with §112 ¶ 2 if one of ordinary skill in the art would understand what is being claimed when the claim is read in light of the patent specification ...If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, section 112 demands no more...

It matters only whether one skilled in the art would understand the term "solution". Applicants' position is that it borders on preposterous to consider that a skilled person in the pertinent art (for example, a pharmaceutical formulations chemist in the instant case) would not understand the term or otherwise find it imprecise or indefinite. No basis has been provided as to why subparagraphs (c) and/or (d) above are indefinite by reason of the term "solution". If the scope of subject matter embraced by a claim is clear, and if an Applicant has not otherwise indicated that he intends that claim to be of a different scope, then the claim does particularly point out and distinctly claim the subject matter which the Applicant regards as his invention." In Re Borkowski, 164 U.S.P.Q. 642, at 645-646 (C.C.P.A. 1970). The Examiner has provided no factual basis supporting why the term "solution" would render the claim unclear, not understandable, or otherwise indefinite.

Again, Applicants respectfully submit they are in compliance with 35 U.S.C. §112, second paragraph, and respectfully request withdrawal of the rejection.

The §102 rejection over Okada

Per paragraphs 4 and 5 of the Office Action, claims 1-2, 12-15, 18, 25-31, 41-44, 47, 54-59, 69-72, 75, 82-87, 92, 95, 102, 104-107, 112, 115, 122, 124-127, 132, 135 and 142-145 continue to be rejected under 35 U.S.C. 102(b) as being anticipated by Okada et al. (US 5,496,561). The Examiner stated, in pertinent part:

Okada is relevant to the examined claims and the previous rejection applies here. Applicants emphatically traverse the rejection of the claims as being anticipated by Okada on the grounds that Okada does not describe a composition that comprises solubility improved form of a drug and one of the

cellulose polymers required by the claims. Applicants further state; "the fact that some of the individual elements (e.g., drugs generally and some of Applicants' polymers) disclosed randomly in Okada might be appropriately combined with applicants disclosure is insufficient to support the rejection because there is no written description or enablement in Okada of Applicants'invention." In summary applicants traverse Okada by stating that Okada does not disclose the instant composition and that the composition as amended require a physical mixture of the drug and the polymer, which applicants say is not disclosed by Okada.

6. Applicants' arguments filed 01/24/2005 have been fully considered but they are not persuasive.

The generic claims are directed to a composition that comprises a drug in a solubility improved form, a concentration enhancing polymer and the composition is not a dispersion and the claims further limit the polymers to that recited. It is respectfully noted that the composition requires one of the polymers recited and not all of the polymers recited. Claim 2 directs the solubility-improved drug to be a crystalline drug. The Okada reference is not combined with applicants disclosure, rather Okada discloses the composition.

Okada discloses a composition that comprises a crystalline drug and cellulose acetate phthalate and cellulose acetate phthalate is one of the polymers listed/recited. Therefore, the rejection is proper. It is respectfully noted that applicants on page 29 of the amendment filed 01/24/05, state that it does not matter how a composition is made and that what matters is the composition itself in a composition. Thus the process of preparing the composition by mixing is not critical in the composition. Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. "[E]ven though produce-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 277 USPQ 964, 966 (Fed. Cir. 1985). [Office Action, pages 3-5]

Applicants continue to traverse the rejection. It is Applicants' position that (1) Applicants' claims define a composition outside the scope of Okada's disclosure because Okada does not disclose a physical mixture of a low solubility drug and one of Applicants' required concentration-enhancing polymer and (2) Okada does not disclose a composition otherwise (e.g., in any of the Okada examples) within the scope of Applicants' claims.

Applicants traverse the Examiner's position that Okada constitutes an anticipation of Applicants' claims, especially the comment that

The Okada reference is not combined with applicants disclosure, rather Okada discloses the composition. [Page 4, lines 10 and 11 of the Office Action]

There is no composition specifically disclosed or enabled in Okada that combines any drug in a solubility-improved form with one of the cellulosic ionizable polymers required in Applicants' claims. The Examiner stated (Office Action, page 4, 9th and 10th lines from bottom) that:

Okada discloses a composition that comprises a crystalline drug and cellulose acetate phthalate and cellulose acetate phthalate is one of the polymers listed/recited.

To the contrary, Okada discloses no such composition. Okada discloses cellulose acetate phthalate (CAP) as part of a list at column 4, lines 22-23, as a polymer that is useful for making a membrane layer, but does not disclose any actual composition containing CAP. He mentions the word "crystalline" once at column 3, line 32. There is never an indication that a crystalline form must in fact be a solubility-improved form, or that it must be in combination with one of the polymers specifically required by Applicants.

Okada examples 7 and 9 disclose drug salts, but neither salt is combined with one of Applicants' required cellulosic ionizable polymers. Nowhere else does Okada disclose a physical mixture of a solubility-improved drug with any of the polymers required by Applicants' claims.

The mere fact that Okada mentions cellulose acetate phthalate, CAP, at column 4, lines 22-23 does nothing to change the fact that Okada is non-anticipating. First, no composition of any kind comprising a solubility-improved drug in combination with CAP is disclosed in Okada. Second, CAP is cited for use as a water insoluble high polymer in making membrane layers, not for combining with a solubility-improved drug in a physical mixture. Membranes and coatings in a drug dosage form do not constitute "physical mixtures". Applicants make that clear in their specification at page 10, line 23 to page 11, line 12:

The solid compositions of the present invention are generally combinations comprising the solubility-improved form and concentration-enhancing polymer. **“Combination” as used herein means that the solubility-improved form and concentration-enhancing polymer may be in physical contact with each other or in close proximity but without the necessity of being physically mixed.** For example, the solid composition may be in the form of a multi-layer tablet, as known in the art, wherein one or more layers comprises the solubility-improved form and one or more different layers comprises the concentration-enhancing polymer. Yet another example may constitute a coated tablet wherein either the solubility-improved form of the drug or the concentration-enhancing polymer or both may be present in the tablet core and the coating may comprise the solubility-improved form or the concentration-enhancing polymer or both. **Alternatively, the combination can be in the form of a simple dry physical mixture wherein both the solubility-improved form and concentration-enhancing polymer are mixed in particulate form and wherein the particles of each, regardless of size, retain the same individual physical properties that they exhibit in bulk.** Any conventional method used to mix the polymer and drug together such as physical mixing and dry or wet granulation, which does not substantially convert the drug and polymer to a molecular dispersion, may be used. [Emphasis supplied]

Clearly Applicants definitions differentiate their physical mixture of a solubility-improved drug and a specific polymer from Okada, which never discloses a physical mixture of a drug with any polymer specified in Applicants' claims.

Applicants' submit the Examiner has simply taken some of the individual elements (e.g., the word “crystalline”, the disclosure of CAP) disclosed randomly in Okada, juxtaposed them appropriately using Applicants' specification as a guide, and then alleged that Okada is anticipatory. That juxtaposition is by the Examiner, however, not Okada. Okada, aside from never disclosing an actual composition containing CAP, mentions CAP only as a membrane material, not for use in making a drug/CAP physical mixture. It is thus Applicants' position that Okada does not disclose the elements required by Applicants' claims - - a solubility-improved form of a drug physically mixed with one or more of the concentration-enhancing polymers specifically named in the claims.

The Examiner is also reminded that Applicants' claims explicitly require that the maximum drug concentration (claim 1), the area under the AUC curve (claim 30), or the relative bioavailability (claim 58) be enhanced over that for a control composition not containing polymer. That requires that the concentration-enhancing polymer dissolve along with the drug so that it can inhibit precipitation of dissolved drug (page 14, lines 24-27). Such a composition is, on its face, completely distinct from Okada. The stated purpose of Okada is to make a controlled release dosage form by forming a rate-limiting membrane around a central core. Such a membrane performs its function of controlling release by remaining intact, not by dissolving as implicitly required in Applicants' invention. Okada specifically

states that the high polymer used to make his membranes is water insoluble (column 4, line 11). A physical mixture of drug and polymer, which functioned by dissolving (as it must in order to enhance concentration) would defeat the purpose of Okada's invention.

The Examiner is accordingly respectfully urged to reconsider and withdraw the rejection. The skilled art worker, having read Applicants' specification and being aware of the definitions employed therein, would readily realize that Okada does not disclose a solubility-improved drug physically mixed with any of the polymers specifically named; rather one skilled in the art would readily realize that Okada discloses only controlled release dosage forms containing a drug and water-insoluble polymer, i.e., as a drug and a polymer membrane or coating, wherein the drug and polymer are merely in close proximity.

The §102 and §103 Rejections Over Bymaster

Claims 1, 30, 58, 86, 126, and 156-161 were rejected under §102(e) as anticipated by Bymaster, US 6,147,072. Claims 146, 147, 151-155, 162, and 163 were rejected under §103(a) as obvious over Bymaster. Bymaster is insufficient to support either rejection, for the reasons that follow.

Bymaster, at most, discloses that some of the polymeric components useful in Applicants' invention are known. But Bymaster, like Okada, never discloses, describes or suggests a composition in which one of the specific polymers in Applicants' claims is physically mixed with a solubility-improved drug. Bymaster simply discloses certain polymers for use in making an enteric dosage form, i.e., one coated with an enteric polymer that will allow it to pass through the (acid) upper GI tract. But, enterically coated dosage forms are not physical mixtures. Because Bymaster never discloses a composition within the scope of Applicants' claims, Bymaster cannot anticipate.

Bymaster never otherwise discloses anything relating to any composition that is a physical mixture of one of Applicants' polymers and a solubility-improved drug. There is not even a bare suggestion to make, or any motivation for making, such a physical mixture. It is well accepted that in order for an obviousness rejection to lie, the prior art must in some way supply a suggestion to do that which Applicant has invented, and must also provide a reasonable expectation of success. . American Hospital Supply Corp. v. Travenol Laboratories, Inc., 223 USPQ 577, 582 (Fed. Cir. 1984). The Federal Circuit has explained the proper test:

The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out **and would have a reasonable likelihood of success**, viewed in light of the

prior art. **Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure** (emphasis added).

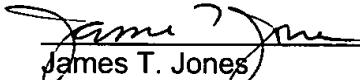
In re Dow Chemical Co., 5 USPQ.2d 1529, 1531 (Fed. Cir. 1988); Amgen, Inc. V. Chugai Pharmaceutical Co. Ltd. 18 USPQ.2d 1016. 1022-23 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991). Bymaster suggests neither the composition, any reason for making one, or any expectation of success. Thus Bymaster is insufficient, in fact and in law, to support an obviousness rejection.

It is accordingly respectfully requested that the rejections over Bymaster be withdrawn.

In view of the foregoing comments and amendments, this case is believed to be in condition for allowance, and a Notice of Allowance is courteously solicited.

Respectfully submitted,

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CLAIMS

1. (currently amended) A composition comprising:

- (a) a drug in a pharmaceutically acceptable solubility-improved form; and
- (b) a concentration-enhancing polymer combined with said solubility-improved form in a sufficient amount so that said composition provides, after introduction to a use environment, a maximum concentration of said drug in said use environment that is at least 1.25-fold an equilibrium concentration of said drug in said use environment, and a concentration of said drug in said use environment that exceeds said equilibrium concentration for a longer time than the concentration of said drug in said use environment provided by a control composition exceeds said equilibrium concentration, wherein said control composition is free from said concentration-enhancing polymer and comprises an equivalent quantity of said drug in said solubility-improved form,

wherein

said composition is not a dispersion;

said drug has an aqueous solubility less than about 1 mg/mL;

said concentration-enhancing polymer is a cellulosic ionizable polymer selected from the group consisting of cellulose acetate phthalate, methyl cellulose acetate phthalate, ethyl cellulose acetate phthalate, hydroxypropyl cellulose acetate phthalate, hydroxypropyl methyl cellulose acetate phthalate, hydroxypropyl cellulose acetate phthalate succinate, cellulose propionate phthalate, hydroxypropyl cellulose butyrate phthalate, hydroxypropyl methyl cellulose phthalate, hydroxypropyl methyl cellulose acetate succinate, cellulose acetate trimellitate, methyl cellulose acetate trimellitate, ethyl cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate, hydroxypropyl methyl cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate succinate, cellulose propionate trimellitate, cellulose butyrate trimellitate, cellulose acetate terephthalate, cellulose acetate isophthalate, cellulose acetate pyridinedicarboxylate, salicylic acid cellulose acetate, hydroxypropyl salicylic acid cellulose acetate, ethylbenzoic acid cellulose acetate, hydroxypropyl ethylbenzoic acid cellulose acetate, ethyl phthalic acid cellulose acetate, ethyl

nicotinic acid cellulose acetate, carboxymethyl ethyl cellulose and ethyl picolinic acid cellulose acetate; and

said drug and said polymer are combined as a simple physical mixture.

2. (original) The composition of claim 1 wherein said drug in said solubility-improved form is a crystalline highly soluble salt form of said drug.

3. (withdrawn) The composition of claim 1 wherein said drug in said solubility-improved form is a high-energy crystalline form of said drug.

4. (withdrawn) The composition of claim 1 wherein said drug in said solubility-improved form is amorphous.

5. (withdrawn) The composition of claim 1 wherein said drug in said solubility-improved form is a composition comprising a mixture of said drug and a solubilizing agent.

6. (withdrawn) The composition of claim 5 wherein said solubilizing agent is selected from the group consisting of surfactants, pH control agents, glycerides, partial glycerides, glyceride derivatives, polyoxyethylene and polyoxypropylene ethers and their copolymers, sorbitan esters, polyoxyethylene sorbitan esters, alkyl sulfonates, and cyclodextrins.

7. (withdrawn) The composition of claim 6 wherein said pH control agents are selected from the group consisting of buffers, organic acids, organic acid salts, organic and inorganic bases, and organic and inorganic base salts.

8. (withdrawn) The composition of claim 5 wherein said drug is basic and said solubilizer is an organic acid selected from the group consisting of adipic acid, citric acid, fumaric acid, malic acid, succinic acid, tartaric acid, erythorbic acid, maleic acid, L-aspartic acid, L-glutamic acid, tannic acid, and D,L-tyrosine.

9. (withdrawn) The composition of claim 1 wherein said drug in said solubility-improved form is a solution of a drug substantially dissolved in a liquid to a

concentration that is at least 10-fold said equilibrium concentration of said drug in said use environment.

10. (withdrawn) The composition of claim 9 wherein said liquid is selected from the group consisting of water-immiscible triglyceride vegetable oils, water-immiscible refined and synthetic and semisynthetic oils, mono-, di- and tri-glycerides, water-miscible alcohols, and water-miscible polyethyleneglycols.

11. (withdrawn) The composition of claim 9 wherein said liquid comprises water and a water-soluble solubilizer.

12. (original) The composition of claim 1 wherein said use environment is *in vivo*.

13. (original) The composition of claim 12 wherein said use environment is selected from the group consisting of the GI tract, subcutaneous space, vaginal tract, pulmonary tract, arterial and venous blood vessels, and intramuscular tissue of an animal.

14. (original) The composition of claim 1 wherein said use environment is *in vitro*.

15. (original) The composition of claim 1 wherein said concentration-enhancing polymer has a hydrophobic portion and a hydrophilic portion.

16. (canceled)

17. (canceled)

18. (previously amended) The composition of claim 1 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate succinate, hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate, and cellulose acetate trimellitate.

19. (withdrawn) The composition of claim 1 wherein said polymer is a non-ionizable cellulosic polymer.

20. (withdrawn) The composition of claim 19 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate, hydroxypropyl methyl cellulose, hydroxypropyl cellulose, methyl cellulose, hydroxyethyl methyl cellulose, hydroxyethyl cellulose acetate, and hydroxyethyl ethyl cellulose.

21. (withdrawn) The composition of claim 1 wherein said polymer is an ionizable, non-cellulosic polymer.

22. (withdrawn) The composition of claim 21 wherein said polymer is selected from the group consisting of carboxylic acid functionalized polymethacrylates, carboxylic acid functionalized polyacrylates, amine-functionalized polyacrylates, amine-fuctinoalized polymethacrylates, proteins, and carboxylic acid functionalized starches.

23. (withdrawn) The composition of claim 1 wherein said polymer is a non-ionizable, non-cellulosic polymer.

24. (withdrawn) The composition of claim 23 wherein said polymer is selected from the group consisting of polyvinyl alcohols that have at least a portion of their repeat units in the unhydrolyzed (vinyl acetate) form, polyvinyl alcohol polyvinyl acetate copolymers, polyethylene glycol, polyethylene glycol polypropylene glycol copolymers, polyvinyl pyrrolidone, polyethylene polyvinyl alcohol copolymers, and chitin.

25. (original) The composition of claim 1 wherein said composition provides a dissolution area under the concentration versus time curve in a use environment for a period of at least 90 minutes during the 1200 minutes immediately following introduction to said use environment that is at least 1.25-fold the corresponding area under the curve provided by said control composition.

26. (original) The composition of claim 1 wherein said maximum concentration of said drug in said use environment is at least 2-fold said equilibrium concentration.

27. (original) The composition of claim 1 wherein said composition provides a relative bioavailability of at least 1.25.

28. (original) The composition of claim 1 wherein said composition provides a maximum concentration in said use environment that is at least 1.25-fold the maximum drug concentration in said use environment provided by said control composition.

29. (original) The composition of claim 1 wherein said drug is selected from antihypertensives, antianxiety agents, anticlotting agents, anticonvulsants, blood glucose-lowering agents, decongestants, antihistamines, antitussives, antineoplastics, beta blockers, anti-inflammatories, antipsychotic agents, cognitive enhancers, cholesterol-reducing agents, antiobesity agents, autoimmune disorder agents, anti-impotence agents, antibacterial and antifungal agents, hypnotic agents, anti-Parkinsonism agents, anti-Alzheimer's disease agents, antibiotics, anti-depressants, and antiviral agents.

30. (currently amended) A composition comprising:

- (a) a drug in a pharmaceutically acceptable solubility-improved form; and
- (b) a concentration-enhancing polymer combined with said drug in a sufficient amount so that said composition provides, after introduction to a use environment, a dissolution area under the concentration versus time curve in said use environment for a period of at least 90 minutes during the 1200 minutes immediately following introduction to said use environment that is at least 1.25-fold the corresponding area under the curve provided by a control composition, wherein said control composition is free from said concentration-enhancing polymer and comprises an equivalent quantity of said drug in said solubility-improved form,

wherein

said composition is not a dispersion;

said drug has an aqueous solubility less than about 1 mg/mL;

said concentration-enhancing polymer is a cellulosic ionizable polymer selected from the group consisting of cellulose acetate phthalate, methyl cellulose acetate phthalate, ethyl cellulose acetate phthalate, hydroxypropyl cellulose acetate

phthalate, hydroxypropyl methyl cellulose acetate phthalate, hydroxypropyl cellulose acetate phthalate succinate, cellulose propionate phthalate, hydroxypropyl cellulose butyrate phthalate, hydroxypropyl methyl cellulose phthalate, hydroxypropyl methyl cellulose acetate succinate, cellulose acetate trimellitate, methyl cellulose acetate trimellitate, ethyl cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate, hydroxypropyl methyl cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate succinate, cellulose propionate trimellitate, cellulose butyrate trimellitate, cellulose acetate terephthalate, cellulose acetate isophthalate, cellulose acetate pyridinedicarboxylate, salicylic acid cellulose acetate, hydroxypropyl salicylic acid cellulose acetate, ethylbenzoic acid cellulose acetate, hydroxypropyl ethylbenzoic acid cellulose acetate, ethyl phthalic acid cellulose acetate, ethyl nicotinic acid cellulose acetate, carboxymethyl ethyl cellulose and ethyl picolinic acid cellulose acetate; and

said drug and said polymer are combined as a simple physical mixture.

31. (original) The composition of claim 30 wherein said drug in said solubility-improved form is a crystalline highly soluble salt form of said drug.

32. (withdrawn) The composition of claim 30 wherein said drug in said solubility-improved form is a high-energy crystalline form of said drug.

33. (withdrawn) The composition of claim 30 wherein said drug in said solubility-improved form is amorphous.

34. (withdrawn) The composition of claim 30 wherein said drug in said solubility-improved form is a composition comprising a mixture of said drug and a solubilizing agent.

35. (withdrawn) The composition of claim 34 wherein said solubilizing agent is selected from the group consisting of surfactants, pH control agents, glycerides, partial glycerides, glyceride derivatives, polyoxyethylene and polyoxypropylene ethers and their copolymers, sorbitan esters, polyoxyethylene sorbitan esters, carbonate salts, alkyl sulfonates, and cyclodextrins.

36. (withdrawn) The composition of claim 35 wherein said pH control agents are selected from the group consisting of buffers, organic acids, organic acid salts, organic and inorganic bases, and organic and inorganic base salts.

37. (withdrawn) The composition of claim 34 wherein said drug is basic and said solubilizer is an organic acid selected from the group consisting of adipic acid, citric acid, fumaric acid, malic acid, succinic acid, tartaric acid, erythorbic acid, maleic acid, L-aspartic acid, L-glutamic acid, tannic acid, and D,L-tyrosine.

38. (withdrawn) The composition of claim 30 wherein said drug in said solubility-improved form is a solution of a drug substantially dissolved in a liquid to a concentration that is at least 10-fold said equilibrium concentration of said drug in said use environment.

39. (withdrawn) The composition of claim 38 wherein said liquid is selected from the group consisting of water-immiscible triglyceride vegetable oils, water-immiscible refined and synthetic and semisynthetic oils, mono-, di-, and tri-glycerides, water-miscible alcohols, and water-miscible polyethyleneglycols.

40. (withdrawn) The composition of claim 38 wherein said liquid comprises water and a water-soluble solubilizer.

41. (original) The composition of claim 30 wherein said use environment is *in vivo*.

42. (original) The composition of claim 41 wherein said use environment is selected from the group consisting of the GI tract, subcutaneous space, vaginal tract, pulmonary tract, arterial and venous blood vessels, and intramuscular tissue of a mammal.

43. (original) The composition of claim 30 wherein said use environment is *in vitro*.

44. (original) The composition of claim 30 wherein said concentration-enhancing polymer has a hydrophobic portion and a hydrophilic portion.

45. (canceled)

46. (canceled)

47. (previously amended) The composition of claim 30 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate succinate, hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate, and cellulose acetate trimellitate.

48. (withdrawn) The composition of claim 30 wherein said polymer is a non-ionizable cellulosic polymer.

49. (withdrawn) The composition of claim 48 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate, hydroxypropyl methyl cellulose, hydroxypropyl cellulose, methyl cellulose, hydroxyethyl methyl cellulose, hydroxyethyl cellulose acetate, and hydroxyethyl ethyl cellulose.

50. (withdrawn) The composition of claim 30 wherein said polymer is an ionizable, non-cellulosic polymer.

51. (withdrawn) The composition of claim 50 wherein said polymer is selected from the group consisting of carboxylic acid functionalized polymethacrylates, carboxylic acid functionalized polyacrylates, amine-functionalized polyacrylates, amine-fuctinoalized polymethacrylates, proteins, and carboxylic acid functionalized starches.

52. (withdrawn) The composition of claim 30 wherein said polymer is a non-ionizable, non-cellulosic polymer.

53. (withdrawn) The composition of claim 52 wherein said polymer is selected from the group consisting of polyvinyl alcohols that have at least a portion of their repeat units in the unhydrolyzed (vinyl acetate) form, polyvinyl alcohol polyvinyl acetate copolymers, polyethylene glycol, polyethylene glycol polypropylene glycol copolymers, polyvinyl pyrrolidone, polyethylene polyvinyl alcohol copolymers, and chitin.

54. (original) The composition of claim 30 wherein said composition provides a maximum concentration of said drug in said use environment that is at least 1.25-fold said equilibrium concentration of said drug provided by said control.

55. (original) The composition of claim 30 wherein said composition provides a relative bioavailability of at least 1.25-fold.

56. (original) The composition of claim 30 wherein said drug is selected from antihypertensives, antianxiety agents, anticlotting agents, anticonvulsants, blood glucose-lowering agents, decongestants, antihistamines, antitussives, antineoplastics, beta blockers, anti-inflammatories, antipsychotic agents, cognitive enhancers, cholesterol-reducing agents, antiobesity agents, autoimmune disorder agents, anti-impotence agents, antibacterial and antifungal agents, hypnotic agents, anti-Parkinsonism agents, anti-Alzheimer's disease agents, antibiotics, anti-depressants, and antiviral agents.

57. (original) The composition of claim 30 wherein said drug concentration provided by said composition is greater than the equilibrium concentration of said drug for at least 15 minutes.

58. (currently amended) A composition comprising:

- (a) a drug in a pharmaceutically acceptable solubility-improved form; and
- (b) a concentration-enhancing polymer combined with said drug in a sufficient amount so that said composition provides, after introduction to a use environment, a relative bioavailability of at least 1.25 relative to a control composition that is free from said concentration-enhancing polymer and comprises an equivalent quantity of said drug in said solubility-improved form,

wherein

said composition is not a dispersion;

said drug has an aqueous solubility less than about 1 mg/mL;

said concentration-enhancing polymer is a cellulosic ionizable polymer selected from the group consisting of cellulose acetate phthalate, methyl cellulose acetate phthalate, ethyl cellulose acetate phthalate, hydroxypropyl cellulose acetate

phthalate, hydroxypropyl methyl cellulose acetate phthalate, hydroxypropyl cellulose acetate phthalate succinate, cellulose propionate phthalate, hydroxypropyl cellulose butyrate phthalate, hydroxypropyl methyl cellulose phthalate, hydroxypropyl methyl cellulose acetate succinate, cellulose acetate trimellitate, methyl cellulose acetate trimellitate, ethyl cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate, hydroxypropyl methyl cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate succinate, cellulose propionate trimellitate, cellulose butyrate trimellitate, cellulose acetate terephthalate, cellulose acetate isophthalate, cellulose acetate pyridinedicarboxylate, salicylic acid cellulose acetate, hydroxypropyl salicylic acid cellulose acetate, ethylbenzoic acid cellulose acetate, hydroxypropyl ethylbenzoic acid cellulose acetate, ethyl phthalic acid cellulose acetate, ethyl nicotinic acid cellulose acetate, carboxymethyl ethyl cellulose and ethyl picolinic acid cellulose acetate; and

said drug and said polymer are combined as a simple physical mixture.

59. (original) The composition of claim 58 wherein said drug in said solubility-improved form is a crystalline highly soluble salt form of said drug.

60. (withdrawn) The composition of claim 58 wherein said drug in said solubility-improved form is a high energy crystalline form of said drug.

61. (withdrawn) The composition of claim 58 wherein said drug in said solubility-improved form is amorphous.

62. (withdrawn) The composition of claim 58 wherein said drug in said solubility-improved form is a composition comprising a mixture of said drug and a solubilizing agent.

63. (withdrawn) The composition of claim 62 wherein said solubilizing agent is selected from the group consisting of surfactants, pH control agents, glycerides, partial glycerides, glyceride derivatives, polyoxyethylene and polyoxypropylene ethers and their copolymers, sorbitan esters, polyoxyethylene sorbitan esters, carbonate salts, alkyl sulfonates, and cyclodextrins.

64. (withdrawn) The composition of claim 63 wherein said pH control agents are selected from the group consisting of buffers, organic acids, organic acid salts, organic and inorganic bases, and organic and inorganic base salts.

65. (withdrawn) The composition of claim 62 wherein said drug is basic and said solubilizer is an organic acid selected from the group consisting of adipic acid, citric acid, fumaric acid, malic acid, succinic acid, tartaric acid, erythorbic acid, maleic acid, L-aspartic acid, L-glutamic acid, tannic acid, and D,L-tyrosine.

66. (withdrawn) The composition of claim 58 wherein said drug in said solubility-improved form is a solution of a drug substantially dissolved in a liquid to a concentration that is at least 10-fold said equilibrium concentration of said drug in said use environment.

67. (withdrawn) The composition of claim 66 wherein said liquid is selected from the group consisting of water-immiscible triglyceride vegetable oils, water-immiscible refined and synthetic and semisynthetic oils, mono-, di-, and tri-glycerides, water-miscible alcohols, and water-miscible polyethyleneglycols.

68. (withdrawn) The composition of claim 66 wherein said liquid comprises water and a water-soluble solubilizer.

69. (original) The composition of claim 58 wherein said use environment is *in vivo*.

70. (original) The composition of claim 88 wherein said use environment is selected from the group consisting of the GI tract, subcutaneous space, vaginal tract, pulmonary tract, arterial and venous blood vessels, and intramuscular tissue of an animal.

71. (original) The composition of claim 58 wherein said use environment is *in vitro*.

72. (original) The composition of claim 58 wherein said concentration-enhancing polymer has a hydrophobic portion and a hydrophilic portion.

73. (canceled)

74. (canceled)

75. (previously amended) The composition of claim 58 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate succinate, hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate, and cellulose acetate trimellitate.

76. (withdrawn) The composition of claim 58 wherein said polymer is a non-ionizable cellulosic polymer.

77. (withdrawn) The composition of claim 76 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate, hydroxypropyl methyl cellulose, hydroxypropyl cellulose, methyl cellulose, hydroxyethyl methyl cellulose, hydroxyethyl cellulose acetate, and hydroxyethyl ethyl cellulose.

78. (withdrawn) The composition of claim 58 wherein said polymer is an ionizable, non-cellulosic polymer.

79. (withdrawn) The composition of claim 78 wherein said polymer is selected from the group consisting of carboxylic acid functionalized polymethacrylates, carboxylic acid functionalized polyacrylates, amine-functionalized polyacrylates, amine-functionalized polymethacrylates, proteins, and carboxylic acid functionalized starches.

80. (withdrawn) The composition of claim 58 wherein said polymer is a non-ionizable, non-cellulosic polymer.

81. (withdrawn) The composition of claim 80 wherein said polymer is selected from the group consisting of polyvinyl alcohols that have at least a portion of their repeat units in the unhydrolyzed (vinyl acetate) form, polyvinyl alcohol polyvinyl acetate

copolymers, polyethylene glycol, polyethylene glycol polypropylene glycol copolymers, polyvinyl pyrrolidone, polyethylene polyvinyl alcohol copolymers, and chitin.

82. (original) The composition of claim 58 wherein said composition provides a maximum concentration of said drug in said use environment that is at least 1.25-fold said equilibrium concentration of said drug provided by said control.

83. (original) The composition of claim 58 wherein said composition provides a maximum concentration of said drug in said use environment that is at least 2-fold said equilibrium concentration.

84. (original) The composition of claim 58 wherein said drug is selected from antihypertensives, antianxiety agents, anticlotting agents, anticonvulsants, blood glucose-lowering agents, decongestants, antihistamines, antitussives, antineoplastics, beta blockers, anti-inflammatories, antipsychotic agents, cognitive enhancers, cholesterol-reducing agents, antiobesity agents, autoimmune disorder agents, anti-impotence agents, antibacterial and antifungal agents, hypnotic agents, anti-Parkinsonism agents, anti-Alzheimer's disease agents, antibiotics, anti-depressants, and antiviral agents.

85. (original) The composition of claim 58 wherein said drug concentration provided by said composition exceeds the equilibrium concentration of said drug for at least 15 minutes.

86. (currently amended) A method of administering a drug comprising co-administering to a patient in need of said drug:

- (a) a drug in a solubility-improved form; and
- (b) a concentration-enhancing polymer;

wherein

said concentration-enhancing polymer is co-administered with said solubility-improved form in a sufficient amount, so that after introduction to a use environment, a maximum concentration of said drug in said use environment is provided that is at least 1.25-fold an equilibrium concentration of said drug in said use environment provided by a control composition;

a concentration of said drug in said use environment is provided that exceeds said equilibrium concentration for a longer time than the concentration of said drug in said use environment provided by said control composition exceeds said equilibrium concentration;

said control composition is free from said concentration-enhancing polymer and comprises an equivalent quantity of said drug in said solubility-improved form,

(a) and (b) are not administered in a dispersion;

said drug has an aqueous solubility less than about 1 mg/mL;

said concentration-enhancing polymer is a cellulosic ionizable polymer selected from the group consisting of cellulose acetate phthalate, methyl cellulose acetate phthalate, ethyl cellulose acetate phthalate, hydroxypropyl cellulose acetate phthalate, hydroxypropyl methyl cellulose acetate phthalate, hydroxypropyl cellulose acetate phthalate succinate, cellulose propionate phthalate, hydroxypropyl cellulose butyrate phthalate, hydroxypropyl methyl cellulose phthalate, hydroxypropyl methyl cellulose acetate succinate, cellulose acetate trimellitate, methyl cellulose acetate trimellitate, ethyl cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate, hydroxypropyl methyl cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate succinate, cellulose propionate trimellitate, cellulose butyrate trimellitate, cellulose acetate terephthalate, cellulose acetate isophthalate, cellulose acetate pyridinedicarboxylate, salicylic acid cellulose acetate, hydroxypropyl salicylic acid cellulose acetate, ethylbenzoic acid cellulose acetate, hydroxypropyl ethylbenzoic acid cellulose acetate, ethyl phthalic acid cellulose acetate, ethyl nicotinic acid cellulose acetate, carboxymethyl ethyl cellulose and ethyl picolinic acid cellulose acetate; and

said drug and said polymer are combined as a simple physical mixture.

87. (original) The method of claim 86 wherein said drug in said solubility-improved form is a crystalline highly soluble salt form of said drug.

88. (withdrawn) The method of claim 86 wherein said drug in said solubility-improved form is a high-energy crystalline form of said drug.

89. (withdrawn) The method of claim 86 wherein said drug in said solubility-improved form is amorphous.

90. (withdrawn) The method of claim 86 wherein said drug in said solubility-improved form is a composition comprising a mixture of said drug and a solubilizing agent.

91. (withdrawn) The method of claim 86 wherein said drug in said solubility-improved form is a solution of a drug substantially dissolved in a liquid to a concentration that is at least 10-fold an equilibrium concentration of said drug in said use environment.

92. (original) The method of claim 86 wherein said concentration-enhancing polymer has a hydrophobic portion and a hydrophilic portion.

93. (canceled)

94. (canceled)

95. (previously amended) The method of claim 86 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate succinate, hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate, and cellulose acetate trimellitate.

96. (withdrawn) The method of claim 86 wherein said polymer is a non-ionizable cellulosic polymer.

97. (withdrawn) The method of claim 96 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate, hydroxypropyl methyl cellulose, hydroxypropyl cellulose, methyl cellulose, hydroxyethyl methyl cellulose, hydroxyethyl cellulose acetate, and hydroxyethyl ethyl cellulose.

98. (withdrawn) The method of claim 86 wherein said polymer is an ionizable, non-cellulosic polymer.

99. (withdrawn) The method of claim 98 wherein said polymer is selected from the group consisting of carboxylic acid functionalized polymethacrylates, carboxylic acid functionalized polyacrylates, amine-functionalized polyacrylates, amine-fuctinoalized polymethacrylates, proteins, and carboxylic acid functionalized starches.

100. (withdrawn) The method of claim 86 wherein said polymer is a non-ionizable, non-cellulosic polymer.

101. (withdrawn) The method of claim 100 wherein said polymer is selected from the group consisting of polyvinyl alcohols that have at least a portion of their repeat units in the unhydrolyzed (vinyl acetate) form, polyvinyl alcohol polyvinyl acetate copolymers, polyethylene glycol, polyethylene glycol polypropylene glycol copolymers, polyvinyl pyrrolidone, polyethylene polyvinyl alcohol copolymers, and chitin.

102. (original) The method of claim 86 wherein a maximum concentration in said use environment is provided that is at least 1.25-fold the maximum drug concentration in said use environment provided by said control composition.

103. (canceled)

104. (previously amended) The method of claim 86 wherein said drug and said concentration-enhancing polymer are administered at essentially the same time.

105. (original) The method of claim 86 wherein said drug is administered in a composition also comprising said concentration-enhancing polymer.

106. (currently amended) A method of administering a drug comprising co-administering to a patient in need of said drug:

- (a) a drug in a solubility-improved form; and
- (b) a concentration-enhancing polymer;

wherein

said concentration-enhancing polymer is co-administered with said drug in a sufficient amount so that, after introduction to a use environment, a dissolution area under the concentration versus time curve is provided in said use environment for a period of at least 90

minutes during the 1200 minutes immediately following introduction to said use environment that is at least 1.25-fold the corresponding area under the curve provided by a control composition;

said control composition is free from said concentration-enhancing polymer and comprises an equivalent quantity of said drug in said solubility-improved form,

(a) and (b) are not administered in a dispersion;

said drug has an aqueous solubility less than about 1 mg/mL;

said concentration-enhancing polymer is a cellulosic ionizable polymer selected from the group consisting of cellulose acetate phthalate, methyl cellulose acetate phthalate, ethyl cellulose acetate phthalate, hydroxypropyl cellulose acetate phthalate, hydroxypropyl methyl cellulose acetate phthalate, hydroxypropyl cellulose acetate phthalate succinate, cellulose propionate phthalate, hydroxypropyl cellulose butyrate phthalate, hydroxypropyl methyl cellulose phthalate, hydroxypropyl methyl cellulose acetate succinate, cellulose acetate trimellitate, methyl cellulose acetate trimellitate, ethyl cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate, hydroxypropyl methyl cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate succinate, cellulose propionate trimellitate, cellulose butyrate trimellitate, cellulose acetate terephthalate, cellulose acetate isophthalate, cellulose acetate pyridinedicarboxylate, salicylic acid cellulose acetate, hydroxypropyl salicylic acid cellulose acetate, ethylbenzoic acid cellulose acetate, hydroxypropyl ethylbenzoic acid cellulose acetate, ethyl phthalic acid cellulose acetate, ethyl nicotinic acid cellulose acetate, carboxymethyl ethyl cellulose and ethyl picolinic acid cellulose acetate; and said drug and said polymer are combined as a simple physical mixture.

107. (original) The method of claim 106 wherein said drug in said solubility-improved form is a crystalline highly soluble salt form of said drug.

108. (withdrawn) The method of claim 106 wherein said drug in said solubility-improved form is a high-energy crystalline form of said drug.

109. (withdrawn) The method of claim 106 wherein said drug in said solubility-improved form is amorphous.

110. (withdrawn) The method of claim 106 wherein said drug in said solubility-improved form is a composition comprising a mixture of said drug and a solubilizing agent.

111. (withdrawn) The method of claim 106 wherein said drug in said solubility-improved form is a solution of a drug substantially dissolved in a liquid to a concentration that is at least 10-fold an equilibrium concentration of said drug in said use environment.

112. (original) The method of claim 106 wherein said concentration-enhancing polymer has a hydrophobic portion and a hydrophilic portion.

113. (canceled)

114. (canceled)

115. (previously amended) The method of claim 106 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate succinate, hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate, and cellulose acetate trimellitate.

116. (withdrawn) The method of claim 106 wherein said polymer is a non-ionizable cellulosic polymer.

117. (withdrawn) The method of claim 106 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate, hydroxypropyl methyl cellulose, hydroxypropyl cellulose, methyl cellulose, hydroxyethyl methyl cellulose, hydroxyethyl cellulose acetate, and hydroxyethyl ethyl cellulose.

118. (withdrawn) The method of claim 106 wherein said polymer is an ionizable, non-cellulosic polymer.

119. (withdrawn) The method of claim 118 wherein said polymer is selected from the group consisting of carboxylic acid functionalized polymethacrylates, carboxylic acid

functionalized polyacrylates, amine-functionalized polyacrylates, amine-fuctinoalized polymethacrylates, proteins, and carboxylic acid functionalized starches.

120. (withdrawn) The method of claim 106 wherein said polymer is a non-ionizable, non-cellulosic polymer.

121. (withdrawn) The method of claim 120 wherein said polymer is selected from the group consisting of polyvinyl alcohols that have at least a portion of their repeat units in the unhydrolyzed (vinyl acetate) form, polyvinyl alcohol polyvinyl acetate copolymers, polyethylene glycol, polyethylene glycol polypropylene glycol copolymers, polyvinyl pyrrolidone, polyethylene polyvinyl alcohol copolymers, and chitin.

122. (original) The method of claim 106 wherein a maximum concentration in said use environment is provided that is at least 1.25-fold the maximum drug concentration in said use environment provided by said control composition.

123. (canceled)

124. (previously amended) The method of claim 106 wherein said drug and said concentration-enhancing polymer are administered at essentially the same time.

125. (original) The method of claim 106 wherein said drug is administered in a composition also comprising said concentration-enhancing polymer.

126. (currently amended) A method of administering a drug comprising co-administering to a patient in need of said drug:

- (a) a drug in a solubility-improved form; and
- (b) a concentration-enhancing polymer;

wherein

said concentration-enhancing polymer is co-administered with said drug in a sufficient amount so that, after introduction to a use environment, a relative bioavailability is provided of at least 1.25-fold that of a control composition, wherein said control composition is free from said concentration-enhancing polymer and comprises an equivalent quantity of said drug in said solubility-improved form,

(a) and (b) are not administered in a dispersion;

said drug has an aqueous solubility less than about 1 mg/mL;

said concentration-enhancing polymer is a cellulosic ionizable polymer selected from the group consisting of cellulose acetate phthalate, methyl cellulose acetate phthalate, ethyl cellulose acetate phthalate, hydroxypropyl cellulose acetate phthalate, hydroxypropyl methyl cellulose acetate phthalate, hydroxypropyl cellulose acetate phthalate succinate, cellulose propionate phthalate, hydroxypropyl cellulose butyrate phthalate, hydroxypropyl methyl cellulose phthalate, hydroxypropyl methyl cellulose acetate succinate, cellulose acetate trimellitate, methyl cellulose acetate trimellitate, ethyl cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate, hydroxypropyl methyl cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate succinate, cellulose propionate trimellitate, cellulose butyrate trimellitate, cellulose acetate terephthalate, cellulose acetate isophthalate, cellulose acetate pyridinedicarboxylate, salicylic acid cellulose acetate, hydroxypropyl salicylic acid cellulose acetate, ethylbenzoic acid cellulose acetate, hydroxypropyl ethylbenzoic acid cellulose acetate, ethyl phthalic acid cellulose acetate, ethyl nicotinic acid cellulose acetate, carboxymethyl ethyl cellulose and ethyl picolinic acid cellulose acetate; and

said drug and said polymer are combined as a simple physical mixture.

127. (original) The method of claim 126 wherein said drug in said solubility-improved form is a crystalline highly soluble salt form of said drug.

128. (withdrawn) The method of claim 126 wherein said drug in said solubility-improved form is a high-energy crystalline form of said drug.

129. (withdrawn) The method of claim 126 wherein said drug in said solubility-improved form is amorphous.

130. (withdrawn) The method of claim 126 wherein said drug in said solubility-improved form is a composition comprising a mixture of said drug and a solubilizing agent.

131. (withdrawn) The method of claim 126 wherein said drug in said solubility-improved form is a solution of a drug substantially dissolved in a liquid to a

concentration that is at least 10-fold an equilibrium concentration of said drug in said use environment.

132. (original) The method of claim 126 wherein said concentration-enhancing polymer has a hydrophobic portion and a hydrophilic portion.

133. (canceled)

134. (canceled)

135. (previously amended) The method of claim 126 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate succinate, hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate, and cellulose acetate trimellitate.

136. (withdrawn) The method of claim 126 wherein said polymer is a non-ionizable cellulosic polymer.

137. (withdrawn) The method of claim 126 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate, hydroxypropyl methyl cellulose, hydroxypropyl cellulose, methyl cellulose, hydroxyethyl methyl cellulose, hydroxyethyl cellulose acetate, and hydroxyethyl ethyl cellulose.

138. (withdrawn) The method of claim 126 wherein said polymer is an ionizable, non-cellulosic polymer.

139. (withdrawn) The method of claim 138 wherein said polymer is selected from the group consisting of carboxylic acid functionalized polymethacrylates, carboxylic acid functionalized polyacrylates, amine-functionalized polyacrylates, amine-functionalized polymethacrylates, proteins, and carboxylic acid functionalized starches.

140. (withdrawn) The method of claim 126 wherein said polymer is a non-ionizable, non-cellulosic polymer.

141. (withdrawn) The method of claim 140 wherein said polymer is selected from the group consisting of polyvinyl alcohols that have at least a portion of their repeat units in the unhydrolyzed (vinyl acetate) form, polyvinyl alcohol polyvinyl acetate copolymers, polyethylene glycol, polyethylene glycol polypropylene glycol copolymers, polyvinyl pyrrolidone, polyethylene polyvinyl alcohol copolymers, and chitin.

142. (original) The method of claim 126 wherein a maximum concentration in said use environment is provided that is at least 1.25-fold the maximum drug concentration in said use environment provided by said control composition.

143. (original) The method of claim 126 wherein said drug is administered separately from said concentration-enhancing polymer.

144. (original) The method of claim 143 wherein said drug and said concentration-enhancing polymer are administered at essentially the same time.

145. (original) The method of claim 126 wherein said drug is administered in a composition also comprising said concentration-enhancing polymer.

146. (original) An aqueous solution formed by administration of a solid drug in a solubility-improved form and a concentration-enhancing polymer to a use environment, comprising:

- (a) each of said drug and said concentration-enhancing polymer being at least partially dissolved in said solution;
- (b) at least a portion of said dissolved drug being associated with at least a portion of said polymer in a plurality of assemblies of drug and polymer, said assemblies having a size of from about 10 to 1000 nanometers; and
- (c) said solution having a maximum concentration of said drug that is at least 1.25-fold an equilibrium concentration of said drug in said use environment, and a concentration of said drug that exceeds said equilibrium concentration for a longer time than the concentration of said drug in said use environment provided by a control composition exceeds said equilibrium concentration, wherein said control composition is free from said concentration-enhancing polymer and comprises an equivalent quantity of said drug in said solubility-improved form.

147. (original) The solution of claim 146 wherein said drug in said solubility-improved form is a crystalline highly soluble salt form of said drug.

148. (withdrawn) The solution of claim 146 wherein said drug in said solubility-improved form is a high-energy crystalline form of said drug.

149. (withdrawn) The solution of claim 146 wherein said drug in said solubility-improved form is amorphous.

150. (withdrawn) The solution of claim 146 wherein said drug in said solubility-improved form is a composition comprising a mixture of said drug and a solid solubilizing agent.

151. (original) The solution of claim 146 wherein said use environment is *in vivo*.

152. (original) The solution of claim 146 wherein said use environment is selected from the group consisting of the GI tract, subcutaneous space, vaginal tract, pulmonary tract, arterial and venous blood vessels, and intramuscular tissue of an animal.

153. (original) The solution of claim 146 wherein said use environment is *in vitro*.

154. (original) The solution of claim 146 wherein said concentration-enhancing polymer has a hydrophobic portion and a hydrophilic portion.

155. (original) An aqueous solution formed by administration of a drug in a solubility-improved form and a concentration-enhancing polymer to a use environment, comprising:

- (a) each of said drug and said concentration-enhancing polymer being at least partially dissolved in said solution;
- (b) at least a portion of said dissolved drug being associated with at least a portion of said polymer in a plurality of assemblies of drug and polymer, said assemblies having a size of from about 10 to 1000 nanometers;
- (c) said polymer being selected from the group consisting of hydroxypropyl methyl cellulose acetate succinate, cellulose acetate phthalate, hydroxypropyl methyl cellulose phthalate, methyl cellulose acetate phthalate, hydroxypropyl cellulose acetate phthalate, cellulose acetate trimellitate, cellulose acetate terephthalate and cellulose acetate isophthalate; and
- (d) said solution having a maximum concentration of said drug that is at least 1.25-fold an equilibrium concentration of said drug in said use environment, and a concentration of said drug that exceeds said equilibrium concentration for a longer time than the concentration of said drug in said use environment provided by a control composition exceeds said equilibrium concentration, wherein said control composition is free from said concentration-enhancing polymer and comprises an equivalent quantity of said drug in said solubility-improved form.

156. (previously added) The composition of claim 1, wherein said drug is ziprasidone.

157. (previously added) The composition of claim 30, wherein said drug is ziprasidone.

158. (previously added) The composition of claim 58, wherein said drug is ziprasidone.

159. (previously added) The method of claim 86, wherein said drug is ziprasidone.
160. (previously added) The method of claim 106, wherein said drug is ziprasidone.
161. (previously added) The method of claim 126, wherein said drug is ziprasidone.
162. (previously added) The solution of claim 146, wherein said drug is ziprasidone.
163. (previously added) The solution of claim 155, wherein said drug is ziprasidone.